


## Methods and Findings

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### Effect of different doses of S-adenosyl-L-methionine on paracetamol hepatotoxicity in a mouse model

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This study investigated the hepatoprotective effects of N-acetylcysteine and different doses of S-adenosyl-l-methionine after a single intraperitoneal overdose of paracetamol in mice. Plasma concentrations of paracetamol metabolites were also determined. Female mice (Souris OF1 strain) 16 weeks old and weighing 30 g were fasted for 18 h prior to intraperitoneal (i.p.) administration of 375 mg/kg (2.5 mmol/kg) of paracetamol. Experimental subgroups included mice administered paracetamol only (control group), those given of N-acetylcysteine 1 g/kg (6.13 mmol/kg) i.p. immediately after paracetamol overdose (T0) and 6 h after dosing (T6) and those administered S-adenosyl-l-methionine at doses of 20 mg/kg (0.05 mmol/kg) and 1 g/kg (2.5 mmol/kg) i.p. at T0 and T6. Twenty-four hours after paracetamol overdose, mortality and liver necrosis were significantly lower ($p < 0.01$) in mice treated with 2.5 mmol/kg of S-adenosyl-l-methionine and N-acetylcysteine at T0 as compared with the remaining subgroups. Plasma ALT concentrations were significantly lower ($p < 0.01$) in mice treated with 2.5 mmol/kg of S-adenosyl-l-methionine than in those given N-acetylcysteine. Plasma concentrations of paracetamol metabolites showed an increase in the glucuronide conjugate and a decrease in the mercapturic acid conjugate in N-acetylcysteine-treated mice and an overall decrease in the conjugation pathway without changes in the oxidative pathway in S-adenosyl-l-methionine-treated animals. We conclude that S-adenosyl-l-methionine at doses of 1 g/kg (2.5 mmol/kg) i.p. was equally effective as 1 g/kg (6.13 mmol/kg) N-acetylcysteine for preventing hepatotoxicity after paracetamol overdose in mice. S-adenosyl-l-methionine may be a therapeutic alternative to N-acetylcysteine as an antidote for poisoning with paracetamol.